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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,089	03/25/2004	Andrew R. Marks	19240-596 US1	7653

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WilmerHale/Columbia University
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EXAMINER
PACKARD, BENJAMIN J

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
02/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/809,089	MARKS ET AL.	
	Examiner	Art Unit	
	Benjamin Packard	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,15,17,18,25,26,29,30,33-35,43 and 47-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15,17,18,25,26,29,30,33-35,43 and 47-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1pg (11/06/08), 2ogs(11/25/08), 2pgs (01/13/09)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 1/13/09, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

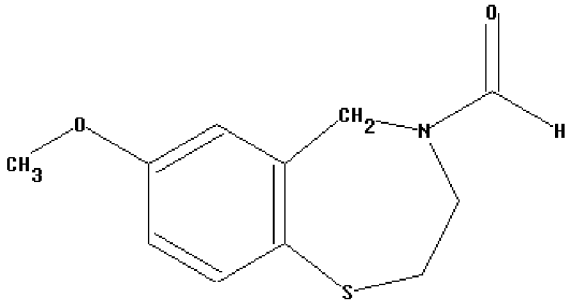
Claim Objections

Claim 29 is objected to because of the following informalities: Amended claim 29 includes the abbreviation "VT". All claimed abbreviations should be spelled out at least once. Appropriate correction is required.

Species Election

Due to a change in Examiner's position on withdrawn claims, claims 13, 15, 17, 18, 25, 26, 29, 30, 33-35, 43 and 47-69 are now also examined.

Additionally, because the claims were amended around the previously elected compound, the search is now expanded to the following compound:



Claim Rejections - 35 USC § 112 - Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13, 15, 17, 18, 29, 30, 33, 43, 47-60, 63, 64, 65, 67, and 69 were/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling of the various methods instantly claimed with compounds S7, S20, S27, and/or S36, does not reasonably provide enablement for the broader class of compounds.

Applicants assert four compounds of formula (g) showing increase of binding to FKBP12.6 to RyR2 are sufficient to show the broader class has similar reactivity.

Examiner notes that the four compounds, while varying the R_4 group and m, do not vary with regards to R1, R2, or R3. It would appear the common core includes a methoxy at the 3 position on the phenyl ring as well as R_2=H and R_3=H. Where the core varies, one of ordinary skill in the art would not have an expectation of success, given the differing structures. Further, the working examples do not appear to have in vitro or in vivo data for where m=1, resulting in a molecule with potentially significantly different polarity properties than the other working examples. Where the enzyme activity requires a “lock and key” relationship, one of ordinary skill in the art would not have an expectation of success where the overall properties of the compound vary (i.e. the polarity).

Claim Rejections - 35 USC § 112 - Indefiniteness

Claims 25, 26, 34, 35, 61 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language.

The claims contain trademark/trade name/lab designations. Where a trademark, trade name, or lab designation is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark, trade name, or lab designation cannot be used properly to identify any particular material or product. A trademark, trade name, lab designation is used to identify a source of goods or an arbitrary reference to a compound, and not the goods themselves. Thus, a trademark, trade name, or lab designation does not identify or describe the goods associated with the trademark or trade name. In the present case, the lab designation is used to identify/describe the instantly claimed compounds and, accordingly, the identification/description is indefinite.

Applicant can overcome this rejection by reciting the chemical names of the compounds.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

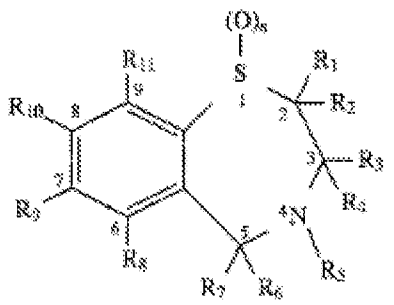
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 15, 18, 29, 30, 33, 43, 47, 48, 50, 53, 54, and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Housley et al (US 5,580,866) in view of Pfmmatter et al (Acta Paediatr 84 (1995) 569-572).

Housley et al teaches a pharmaceutical composition comprising a compound of formula I:



(I)

where n=0, R_1-R_4 are H, R_5 is COR_{13}, R_{13} is H, R_{6-8} and R_{10-11} are H, R_9 is an alkoxy of 1 carbon atom (claim 6) administered from about 1mg to about 1000mg (claim 10) for the treatment of seizures (claim 11), neurological disorders (claim 14), or epilepsy (claim 17). The closest embodiment appears to be 4-acetyl-6-methyl-2,3,4,5-tetrahydro-1,4-benzothiazepine and 4-acetyl-2,3,4,5-tetrahydro-1,4-benzothiazepine.

Housley et al does not teach the disclosed compound as a preferred embodiment and differ from the closes preferred embodiments by the methoxy group attached to the phenol group.

The specific combination of features claimed is disclosed within the broad generic ranges taught by the primary reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the

combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007)(quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected the suggested methoxy group from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

It would reasonably be obvious that the method instantly claimed of increasing binding of FKBP12.6 to RyR2 would occur where the prior art teaches the instantly claimed active step of administering the compound.

Note, claims 29, 30, and 33 are directed to a method of reducing the risk in a subject at risk of developing the instantly claimed condition. It would appear that the method step of administering the drug to any patient, given people are generally at risk of various diseases, would meet the requirement, as disclosed in the primary reference.

Claims 17, 33, 43, 47, 48, 50, 53, 54, 56, 63, 64, 65, 67, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Housley et al (US 5,580,866) in view of Pfmmatter et al (Acta Paediatr 84 (1995) 569-572).

Housley et al is discussed above, but does not disclose the method of treating cardiac arrhythmia.

Pfmmatter et al teaches seizures cardiac arrhythmias can occur with signs and symptoms of a seizure disorder (Introduction first paragraph).

Pfmmatter et al does not teach treating seizures with the instantly claimed compounds.

Where administration of the compounds is taught for the treatment of seizures, one of ordinary skill in the art would reasonably expect the patient populations to overlap given the difficulty in distinguishing between seizure disorders and cardiac arrhythmias as disclosed secondary reference and therefore treat for the possibility of either seizure disorder or cardiac arrhythmia.

Status of the Claims

Compounds of claims 25, 26, 34, 35, 49, 51, 52, 55, 57-62, 66, and 68 appear to be free of the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin Packard whose telephone number is 571-270-3440. The examiner can normally be reached on M-R 8-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Benjamin Packard/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612